

PROKERA®

Patent No. CA 2,623,940 and CA 2,949,643

Product Insert

Description:

PROKERA® is a self-retaining biologic corneal bandage. It is comprised of a cryopreserved amniotic membrane graft fastened to an ophthalmic conformer. The ophthalmic conformer consists of an inner ring and outer ring that serves to maintain space in the orbital cavity and to prevent closure or adhesions. The inner diameter, outer diameter and height of the ophthalmic conformer measure 15.5 mm, 21.6 mm and 2.6 mm, respectively. This product is aseptically processed from tissues obtained from donated human tissue (placentas) according to current Good Tissue Practices (cGTP) and Good Manufacturing Practices (cGMP) regulations established by the US Food & Drug Administration (FDA). PROKERA is a Class II medical device cleared by the FDA and a Class IV medical device regulated by Health Canada.

Donor Eligibility and Summary of Records:

- This tissue was procured from a donor determined to be eligible based on the results of screening and testing. Human Cells, Tissues, and Cellular and Tissue-based Products (HCT/P) donor eligibility and placenta suitability, which is based on the results of donor screening at delivery for infectious, malignant, neurological & auto-immune diseases and for other exposures or social habits, has been determined and documented by TissueTech, Inc.
- A blood specimen, drawn within ± 7 days of donation, has undergone serological testing by a laboratory registered with the FDA to perform donor testing and certified to perform such testing on human specimens in accordance with the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and 42 CFR Part 493, or that has met equivalent requirements as determined by the Centers for Medicare and Medicaid Services (CMS). The donor has been tested for the following infectious diseases and results were non-reactive:
 - HIV-1 & HIV-2 Antibody
 - HIV-1 (RNA-NAT)
 - Hepatitis B Surface Antigen (HBsAg)
 - Hepatitis B Core Antibody (HBcAb)
 - Hepatitis B (HBV, DNA-NAT)
 - Hepatitis C Antibody (HCVAb)
 - Hepatitis C Virus (HCV, RNA-NAT)
 - Syphilis (RPR)
 - HTLV I & II Antibody (HTLV I/II Ab)
 - West Nile Virus (WNV, RNA-NAT)
- Microbial testing has also been performed on the final product to ensure no growth of aerobic, anaerobic or fungal cultures.
- The cell activity in the tissue has been inactivated using our CryoTek® cryopreservation process to reduce the possibility of graft rejection, while retaining the natural biologic properties.
- PROKERA is stored in a medium of Dulbecco's Modified Eagle Medium/Glycerol (1:1) containing 20 $\mu\text{g}/\text{ml}$ Ciprofloxacin and 1.25 $\mu\text{g}/\text{ml}$ Amphotericin B.
- This tissue has been deemed eligible for transplantation based on acceptable screening, serological and microbial test results.
- A Certificate of Compliance regarding the manufacturing, storage, shipping and tracking controls for Bio-Tissue, Inc. products is available upon request.

Indications:

- PROKERA is intended for use in eyes in which ocular surface cells are damaged or underlying stroma is inflamed or scarred and is best suited to prevent adhesion of the eyelid to the ocular surface with the large ophthalmic conformer. Acting as a self-retaining biologic corneal bandage, PROKERA effectively treats superficial corneal surface diseases by suppressing inflammation and related pain, promoting epithelial healing, and avoiding haze.
- PROKERA is inserted between the eyeball and the eyelid to maintain space in the orbital cavity and to prevent lid adhesion to the ocular surface. Placement of the conformer also enables application of the cryopreserved amniotic membrane to the ocular surface without the need for sutures.
- PROKERA is for single-use only in one patient by an ophthalmologist or optometrist.

Contraindications:

- PROKERA should not be used in eyes with glaucoma drainage devices or filtering blebs.

Precautions:

- Do not use PROKERA if the device or packaging is damaged – contact Bio-Tissue immediately if there is any abnormality observed (e.g. device, labeling, shipping, missing information, etc.). Refer to the Customer Feedback section for reporting.
- PROKERA exposed to controlled room temperature (20°C - 25°C) for up to 6 hours may be returned to cold temperature storage in accordance with the Storage section as long as the packaging remains unopened and intact.
- Once the packaging is opened, PROKERA shall either be transplanted or otherwise discarded.
- Do not sterilize or autoclave the product before use.
- Handle PROKERA with care during insertion.

Warnings:

- Do not use on patients with a history of drug reactions to Ciprofloxacin or Amphotericin B.
- As with the use of any human tissue, the possibility of infectious agent transmission cannot be completely eliminated although all screening and microbial testing results for this donor were satisfactory for transplantation.
- It is imperative that the device is stored properly until use. For proper storage instructions refer to the Storage section.
- If the patient cannot close the eyelid, has an incomplete blink or demonstrates any other signs of exposure, address these clinical issues before or at the same time of placing PROKERA.
- If the patient cannot tolerate wearing PROKERA, the device should be removed.

Storage:

It is the responsibility of the Tissue Dispensing Service, Tissue Distribution Intermediary, and/or End-User Clinician to maintain tissue intended for transplant in appropriate storage conditions prior to further distribution or transplantation.

Upon receipt, ensure the shipper is within the validated time indicated on the shipper. Remove the tissue and store accordingly until use :

Location & Temperature	Use After Receipt
-80°C → 4°C (-112°F → 39.2°F) Example: ultra-low temperature freezer, standard freezer, or standard refrigerator	Within the expiration date printed on product packaging (shelf-life is 2 years from date of manufacture)

Place UDI Label Here

See Reverse

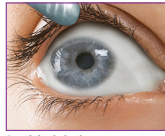
Insertion and Removal Instructions:

- If frozen, allow PROKERA to sit at controlled room temperature (20°C - 25°C) in its original unopened packaging for at least 5 minutes.
- Peel open the lid and handle the tray using aseptic techniques.
- Discard the storage media contained within the tray.
- Thoroughly rinse PROKERA with saline solution while inside the tray to remove the storage media.
- Remove the center retainer piece from the tray to access the PROKERA.
- Patient may experience a temporary foreign body sensation upon insertion.
- Advise patient to minimize contact with eye once PROKERA is placed on the ocular surface.

Insertion



1. Apply topical anesthesia



2. Hold the upper eyelid



3. Ask the patient to look down



4. Insert the PROKERA into the superior fornix

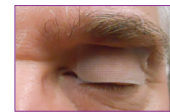


5. Pull lower eyelid down and slide PROKERA under the lower eyelid



6. Check centration under the slit lamp

7. Apply a tape-tarsorrhaphy over the lid crease (as needed)
- Apply appropriate medications (as needed)



Removal



1. Apply topical anesthesia



2. Pull the lower eyelid down



3. Lift lower edge of PROKERA using a cotton swab or blunt forceps



4. Ask the patient to look down



5. Apply gentle pressure on the upper eyelid



6. Slide the PROKERA out

- Upon dissolution of membrane or completion of treatment, remove PROKERA.
- Do not leave in the eye longer than 30 days.

Recipient Records:

It is the responsibility of the Tissue Dispensing Service, Tissue Distribution Intermediary, and/or End-User Clinician to maintain records for the purpose of tracing tissue post-transplantation. The responsible entity should document the disposition (transplanted or discarded) on the Donor and Recipient Information card (DRI), attach one of the provided PROKERA tracking labels to the DRI and mail to Bio-Tissue, Inc. Attach the remaining labels in patient and hospital records. An additional DRI should be provided to the customer in the event that they need to communicate an address change to the manufacturer.

Customer Feedback:

Report any customer feedback, including complaint, error, or accident notification promptly to your local tissue provider or directly to Bio-Tissue, Inc. at (888) 296-8858 or (305) 412-4430.

Adverse Events:

The FDA requires that information be supplied to the product manufacturer for mandatory reporting of adverse events. Possible significant adverse events include microbial infection and transmission of viral disease. The doctor is responsible for immediately reporting any adverse event potentially attributable to the use of PROKERA to Bio-Tissue.

For Adverse Events, complete the following section. Notify via:

Phone: (888) 296-8858 or (305) 412-4430
Fax: (305) 675-3262
Email: Customerfeedback@biotissue.com

Serial Number: _____

Expiration Date: ____/____/____

Doctor Name: _____

Facility Name: _____

Transplant Date: ____/____/____

Diagnosis/Procedure: _____

Site of Use: _____

Point of Contact's Name: _____

Point of Contact's Phone Number: _____

Date Adverse Event was Reported: ____/____/____

Type of Adverse Event: Microbial Infection Transmission of Viral Disease Other

Describe the Adverse Event/Reaction _____

La version française de cette notice est disponible à www.biotissue.com.

Manufactured for Bio-Tissue, Inc. by TissueTech, Inc. 8305 NW 27th St, Suite 101, Doral, FL 33122 USA (888) 296-8858

FEI #: 3009809074
 Health Canada CTO Registration #: 100041